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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/540,024	03/31/2000	Arthur O. Tzianabos	B0801/7169	1627

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Helen C Lockhart
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EXAMINER

LIU, SAMUEL W

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/540,024	Applicant(s) TZIANABOS ET AL.	
	Examiner Samuel W Liu	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19, 37, 61, 63, 65, 67, 101, 103, 104, 106, 108, 111, 127, 138 and 147-163 is/are pending in the application.
- 4a) Of the above claim(s) 37, 61, 63, 65, 67, 101, 103, 104, 106, 108, 111, 127 & 138 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 and 147-163 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Applicants' amendment filed 30 July 2003, which amends claims 1 and 19, and applicants' request for extension of time of three months (filed 30 July 2003) have been entered. Claims 1-19, 37, 61, 63, 65, 67, 101, 103-104, 106, 108, 111, 127, 138 and 147-163 are pending; claims 37, 61, 63, 65, 67, 101, 103-104, 106, 108, 111, 127 and 138 are withdrawn from further consideration by the examiner, as being drawn to a non-elected invention. Claims 1-19 and 147-163 are pending and reexamined in this Office action.

Grounds of objection and/or rejection not explicitly restated and/or set forth below are withdrawn.

Claim Rejections - 35 USC §112, the second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-19 and 147-163 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 19 are unclear as to whether or not repeating charge motifs are or are not the "repeating units" in view of dependent claims (e.g., claim 3) since the specification ambiguously describes repeating units (see page 20, lines 4-20). Of note is that applicants discuss this issue of repeating unit(s) and the repeating charge motif but does not clarify the issue in the claim(s). Also, claim 1 recites "... are separated by an intervening sequence of at least 32 Å"; the recitation is unclear as to what subjects are separated thereof; are the passively charged

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amino moieties within a repeating charge motif separated? or are the repeating charge motifs separated? And, provided that there are > 2 of the repeating motifs thereof, how those repeating motifs will not be separated by the intervening sequence since claim 1 recites ONLY one intervening sequence. See also claims 19 and 155.

The dependent claims are also rejected.

Claim 2 is unclear as to whether or not the non-repeating units refer to (i) the “repeating charge motifs” as compared to the intervening sequence, or (ii) a particular sequence which is neither identical in composition nor identical in order compared to the members of the other units, or (iii) a particular sequence which is identical in composition but not identical in order compared to the members of the other units, or (iv) a particular sequence which has identical composition compared to the members of the other units but is not identical in order compared to the members of the other units. See also claim 147. In addition, claim 2 appears to have the broader statement of limitation, i.e., “non-repeating units” than the recitation “repeating charge motif” of claim 1 from which claim 2 depends, which renders claim 2 indefinite (also see below).

Claim 3 sets forth “the polymer has repeating units” which renders the limitation of claim 3 broader than that of claim 1 from which claim 3 depends; note that that the limitation of “repeating unit” is broader than that of the “repeating charge motifs” (see claim 1), inasmuch as that the repeating unit *encompasses* noncharged “unit”, e.g., monosaccharide or charged “unit”, e.g., nucleotide (see page 20, lines 6-9 of the specification). Thus, the recitation (in *dependent* claim 3) “repeating units” that is a boarder limitation than “repeating charge motifs” (in *independent* claim 1), which renders the claim indefinite. See also claim 148 in view of claim

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19 from which claim 148 depends. Additionally, claim 3 is not apparent as to whether or not the repeating unit encompasses (i) any repeating non-charge motif(unit), or, only the repeating charge motif(unit), or (iii) both the repeating non-charge motif(unit) and the repeating charge motif(unit). See also claim 148.

Claim 6 recites “mixed polymer”; the recitation renders the claim indefinite because only one polymer is recited in claim 1 (see the recitation “a polymer of ...”), and because the specification insufficiently and unclearly define the term “mixed polymer”. Does the mixed polymer refer to a peptide-said polymer or peptide-polysaccharide hybrid molecule? This is not found in claim 6 nor in claim 1.

Claim 11 recites “... are separated by a distance of at least 115 Å”; the recitation is unclear as to what subjects are separated thereof; are the passively charged amino moieties within a repeating charge motif separated ? or are the repeating charge motifs separated? Given that there are > 2 of the repeating motifs thereof, how those repeating motifs will not be separated by the intervening sequence since the claim recites only one intervening sequence. See also claims 12 and 13.

Claim 15 is unclear as to how native would differ from the recitation of “non-native polypeptide” differs from native thereof which the specification does not clearly define.

Claim 18 recites “positive to negative charge ratio of 1:1”; is not clear regarding whether or not the claimed polymer has no net charge because the ratio of positive to negative is 1:1, whether or not the said ratio regards overall positive to negative charges, whether or not the

claimed polymer comprises even number of repeating charge motifs because odd number of repeating charge motifs would not result in the ratio 1:1 thereof.

Response to the rejection under 35 USC 112, the second paragraph

The response file 30 July 2003 argues against the repeating unit and the repeating charge motifs. The applicants' argument has been considered but is unpersuasive. The reasons for this are addressed in the above stated ground of rejection under this section of the statement and/or below.

The response asserts that claims 1 and 19 are not unclear as to whether or not repeating charge motifs are or are not the repeating units in view of the dependent claims as the terms "repeating charge motifs" and repeating units" have definite meaning as provided by specification (see page 9 of the response). The applicants' argument is unpersuasive because the specification vaguely defines the relation between the repeating unit and the repeating charge motif, and because the repeating charge motifs fall into the metes and bounds of the repeating units (see page 8, the 4th paragraph, lines 6-7 of the response). Thus, without identifying the characteristic(s) of the repeating units and the repeating charge motifs, the claims are considered indefinite.

The response asserts that claims 2 and 3 properly impose limitations on claim 1 from which they depend; thus, the claims are not indefinite (see page 9, paragraphs 2-3). The applicants' argument is not persuasive. The response addresses that the claim 1 recitation "repeating charge motifs" are within the metes and bound of claim 2 limitation of "non-repeating unit" (see page 9, the second paragraph as to "The repeating charge motif can reside within the

non-repeating units...”). As stated in the foregoing rejection, the condition that narrower statement of limitation resides in independent claims while the broader statement of limitation in the dependent claim(s) thereof renders the claim(s) indefinite. Herein, the dependent claim 2 has the broader limitation than independent claim 1, as addressed above.

Also, the response argues that claim 6 is not indefinite as the recitation “mixed polymer” has been defined in the specification (see page 19, line 25) wherein the “mixed polymer” is a polymer of heterogeneous backbone composition. The heterogeneous backbone can also refer to isopeptide bond (e.g., amide bond between a carboxyl group of an amino acid residue and ϵ -amine group of lysine residue). The specification appears to refer the “mixed polymer” to a conjugate between (or among) biopolymers, e.g., polypeptide and polynucleotide (see page 19, the last paragraph). In view of the fact that the specification does not explicitly definite what the mixed polymer is and that a polymer (polypeptide) comprising isopeptide bond(s), i.e., a heterogeneous backbone(s), is a homopolymer rather than heteropolymer (mixed polymer), the applicants’ argument is considered not persuasive. Thus, without further clarification, the recitation of “mixed polymer” renders the claim indefinite.

Further, the response argue the issue regarding the recitation “non-native polypeptide” in claim 15, and asserts that the specification (page 7, line 13) has describes the recitation thereof. The applicants’ argument is found not persuasive because the indicated specification does not provide definition for the recitation thereof.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The following is the restatement of the rejection under 35 USC 102(b).

The claims 1-6, 14-16, 18-19, 147-148, 152-160 and 162-163 are rejected under 35 U.S.C. 102(b) as being anticipated by Ferrari, F. A. *et al.* (US Pat. No. 5514581).

Ferrari *et al.* teach a composition comprising a polymer (SEQ ID NO: 102, columns column 5, lines 38-60, and columns 127-128) that is less than 50 KDa and comprises two repeating motifs, each of which contains a positively charged and a negatively charged moiety (**Arg-Gly-Asp**) wherein the two repeating units are separated by a neutral sequence having a distance larger than 32 Å (in view of that a dimension occupied by 8 amino acid residues is equivalent to 32 Å). The above Ferrari's disclosure teaches the all the limitations with regard to the polymer set forth in claim 1.

Claim 1 recites “a pharmaceutical composition”; note that the recitation of “pharmaceutical” has no patentable weight *per se*, absent factual indicia to the contrary; thus, the Ferrari’s patent is applicable to the claim 1 disclosure. The Ferrari’s patent teaches the subject composition for interacting with solution (see column 2, line 34) or combined with organic molecule (see column 48, line 10) for therapeutic use (see column 35, lines 37-39). The teaching therefore meets the limitation “pharmaceutical carrier” in the claim.

Since the repeating unit is identical, Ferrari *et al.* also anticipate the application claims 3, 4 and 148; and since the repeating unit Arg-Gly-Asp has positive to negative charge ratio of 1:1, the Ferrari’s patent is applicable to the application claims 18 and 162.

Ferrari *et al.* teach a polymer (SEQ ID NO: 111, columns 133-134) comprising non-repeating units wherein contain a positively and a negatively charged residues (see **Lys-Gly-Ala-Asp**, and **Arg-Gly-Asp**), as applied to claims 2, 5 and 147 of the instant application.

Ferrari *et al.* teach a composition produced by crosslinking the polymer with other type of polymer or materials, as applied to claims 6, 16 and 160 of the instant application.

Ferrari, *et al.* teach the polymer that is recombinantly synthesized (see abstract), as applied to the application claims 14-15 and 158-159.

Also, Ferrari *et al.* teach (i) a polymer (SEQ ID NO: 66, columns 101-104) that is less than 50 KDa and comprises five repeating motifs, each of which contains positively charged and negatively charged moieties, *e.g.*, the repeating unit I (**Lys-Gly-Asp**) and unit II (**Arg-Gly-Asp**) wherein the two repeating units I and II are contiguous, as applied to the application claim 154; (ii) the polymer wherein the repeating units (**Arg-Gly-Asp**) are separated by at least five neutral

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amino acids, as applied to the application claims 152 and 153; and (iii) the polymer wherein the repeating units (**Arg-Gly-Asp**) are separated by 54 amino acid residues, as applied to the application claims 155-157.

Response to the rejection under 35 USC 102

The response file 30 July 2003 asserts that applicants have amended the claims in such a way, i.e., the instant claims are directed to “pharmaceutical composition comprising the claimed polymer for administering to a subject”, that Ferrari et al. do not anticipate the instantly claimed invention (see page 11). The applicants’ argument is unpersuasive because of the reasons stated in the above rejection and/or below. Note that the recitation of “pharmaceutical” has no patentable weight associated with the use of the composition comprising the claimed polymer which structure and biological activity will not be altered due to the use of the composition thereof. Thus, the Ferrari’s patent is applicable to the disclosure of claims 1 and 19. Furthermore, Ferrari et al. teaches (i) the subject composition for interacting with solution (see column 2, line 34) or combined with organic molecule (see column 48, line 10) which meets the limitation regarding “pharmaceutical carrier” in the claims, and (ii) the composition for therapeutic use, e.g., neovasculation etc. (see column 35, lines 37-39), indicating the disclosed composition is a pharmaceutical composition. Therefore, Ferrari’s teaching anticipates the instant application claims and the rejection is maintained.

The claims 1-6, 14-16, 18-19, 147-148, 152-154, 158-160 and 162-163 are rejected under 35 U.S.C. 102(b) as being anticipated by Rodwell, J. D. *et al.* (US Pat. No.5196510).

Rodwell et al. teach a therapeutic composition comprising the MRU (molecular recognition units) conjugate (see column 20, lines 43-47, and Table III on column 25), wherein the conjugate compound is less than 50 KDa and comprises two repeating motifs, each of which contains a positively charged and a negatively charged moiety (**Arg-Gly-Asp**) wherein the two repeating units are separated by a neutral sequence having a distance larger than 32 Å (in view of that a dimension occupied by 8 amino acid residues is equivalent to 32 Å) (see the ninth polypeptide and the patent claim 1). Thus, above Rodwell's disclosure teaches the all the limitations of the application claims 1, 19 and 163. Since the repeating unit is identical, Rodwell et al. also anticipate the application claims 3, 4 and 148; and since the repeating unit Arg-Gly-Asp has positive to negative charge ratio of 1:1, the Rodwell et al. patent is also applied to the application claims 18 and 162.

Rodwell et al. teach the conjugate compound comprising two structurally distinct/different biopolymers (see the patent claim 1 and column 18, lines 35-57), i.e., the conjugate compound is a mixed biopolymer, which anticipates claims 6, 16 and 160 of the instant application.

Rodwell et al. teach a compound comprising non-repeating units wherein contain a positively (underlined) and a negatively (underlined) charged residues (see KCGLCE and RSFVE of the last polypeptide listed in the patent claim 1), as applied to claims 2, 5 and 147 of the instant application.

Rodwell et al. teach the polymer that is recombinantly synthesized (see column 13, lines 20-40), as applied to the application claims 14-15 and 158-159.

Also, Rodwell et al. teach the conjugate compound wherein the positive and negative charges of repeating charge motifs (e.g. R-G-D) are separated by at least one neutral amino acid (see the 8th peptide of Table III) or by at least five amino acid (see the 9th peptide of Table III), as applied to claims 152-153 of the current application.

Further, Rodwell et al. teach the conjugate compound wherein the positive and negative charges of repeating charge motifs (i.e., YRGDGAPSY) are NOT separated by any neutral amino acid (see the 6th peptide disclosed in the patent claim 1), which anticipates claim 154 of the current application.

The claims 1-2, 5, 14-15, 18, 147, 158-159 and 162 are rejected under 35 U.S.C. 102(e) as being anticipated by Horwitz, D. A. (US Pat. No 6447765) as is evidenced by the known fact disclosed in the publication (Bazan, J. F. (1992) 257, 410-413).

Horwitz teaches a pharmaceutical composition comprising a biopolymer- IL-2 (see column 8, lines 24-28 and lines 60-64, and the patent claim 4), which has characteristics of charge repeating motifs, i.e., Glu-Leu-Lys (ELK) as indicated by Figure 2 of Bazan reference. IL-2 polypeptide, e.g., bovine or human IL-2, is less than 50 KDa and comprises at least two repeating motifs (ELK), each of which contains a positively charged and a negatively charged moiety (**Glu-Leu-Lys**) wherein the two repeating units are separated by a sequence (8 residues) having a distance larger than 32 Å (in view of that a dimension occupied by 8 amino acid residues is equivalent to 32 Å). Thus, Horwitz teaches the limitations with regard to the polymer set forth in claim 1 of the current application. Note that Horwitz's composition is used for

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treating a disease state (see the patent claim 1); thus, the composition is a pharmaceutical composition.

Since the repeating unit is identical, Horwitz also anticipates the application claims 3, 4 and 148; and since the repeating unit "ELK" has positive to negative charge ratio of 1:1, the Ferrari's patent is applicable to the application claims 18 and 162.

Horwitz teaches a polymer (SEQ ID NO: 111, columns 133-134) comprising non-repeating units wherein contain a positively and a negatively charged residues (see DFYVVPKVNATELK, wherein those underlined refer to non-repeating units, as applied to claims 2, 5 and 147 of the instant application.

Also, Horwitz teaches the IL-2 is recombinantly produced (see column 8, lines 63-65), as applied to the application claims 14-15 and 158-159.

The Rejection under 35 USC §103(a) is withdrawn in light of the current applicant' amendment.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703-308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-

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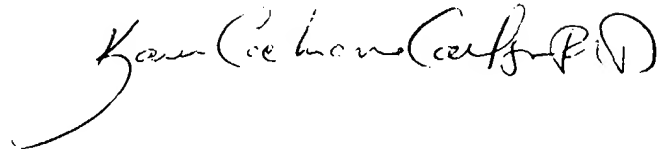
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9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel W. Liu, Ph.D.

November 7, 2003

A handwritten signature in black ink, reading "Karen Cochrane Carlson Ph.D." with a stylized flourish at the end.

KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER